

**REMARKS/ARGUMENTS**

**Disposition of the claims**

Claims 1-42 are pending in the application and stand rejected. Applicants have cancelled claims 1-42 and added new claims 43-64. Applicants respectfully request entry of the new claims.

## **Rejections**

### **The rejection under 35 USC §112, second paragraph**

The Examiner has rejected claims 1-42 under 35 USC §112, second paragraph. Specifically, the Examiner states that the claims "are confusing because it is unclear whether the Applicant actually intended the 'capable of' phrase to be positive limitations in the claims." Applicants have cancelled claims 1-42 and added new claims 43-64. Applicants have written the new claims using language that clearly recites positive limitations in the claims. In light of the cancellation of claims 1-42 and the addition of new claims 43-64, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC §112, second paragraph.

### **The rejection under 35 USC §103(a)**

The Examiner has rejected claims 1-9 and 11-42 under 35 USC §103(a) as being unpatentable over Anderson, et al.(US 2002/0136726). In particular, the Examiner states that "it would be obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Anderson et al and use the ephrin-B2 composition for imaging tumors, causing vascular cell death, delivering an agent to the vasculature, and generating a kit comprising the ephrin-B2 composition...". Applicants respectfully disagree with the Examiner and traverse the rejection as follows.

To establish a *prima facie* case of obviousness, there are three criteria that must be considered and all three of these criteria must be met. Those criteria are 1) a suggestion or motivation to combine references, 2) a reasonable expectation of success, and 3) all claim limitations must be taught. The Examiner's attention is directed to new independent method claims 43, 46 and 49 and kit claims 57, 58, 59, and 62, set forth below (with emphasis added):

43. (New) A method for imaging tumor vasculature in a mammal, comprising:  
a) administering to the mammal a composition which comprises a molecule that detects ephrin-B2 nucleic acid or polypeptide coupled to an imaging agent, wherein the imaging agent is a *radionuclide or a chelate*;

b) allowing the composition to accumulate at the tumor vasculature;  
and

c) detecting the accumulated composition by a *conventional scintillation camera, a gamma camera, a rectilinear scanner, a PET scanner, a SPECT scanner, a MRI scanner, a NMR scanner, an X-ray machine, or an infrared scanner machine so as to image the tumor vasculature.*

46. (New) A method of causing tumor cell death by targeting tumor vasculature comprising administering to a mammal a composition which comprises a molecule that detects ephrin-B2 coupled to an agent that causes tumor cell death, wherein the agent that causes tumor cell death is *carboplatin, cisplatin, vincristine, methotrexate, paclitaxel, docetaxel, 5-fluorouracil, UFT, hydroxyurea, gemcitabine, vinorelbine, irinotecan, tirapazamine, or matrilysin.*

49. (New) A method of causing vascular endothelial cell death by targeting tumor vasculature comprising administering to a mammal a composition which comprises a molecule that detects ephrin-B2 coupled to an agent that causes vascular endothelial cell death, wherein the agent that causes vascular endothelial cell death is *gelonin, ricin A, ricin B, saporin, bryodin 1, bryodin 2, momordin, pokeweed antiviral protein from seeds (PAP-S), trichokirin, or abrin.*

57. (New) A kit for imaging tumor vasculature in a mammal comprising a composition which comprises a molecule that detects ephrin-B2 coupled to an imaging agent, wherein the molecule that detects ephrin-B2 is a nucleic acid and imaging agent is a *radionuclide or a chelate.*

58. (New) A kit for imaging tumor vasculature in a mammal comprising a composition which comprises a molecule that detects ephrin-B2 coupled to an imaging agent, wherein the molecule that detects ephrin-B2 is a polypeptide and imaging agent is a *radionuclide or a chelate.*

59. (New) A kit for causing tumor cell death by targeting tumor vasculature in a mammal comprising a composition which comprises a molecule that detects ephrin-B2 coupled to an agent that causes tumor cell death, wherein the agent that causes

tumor cell death is *carboplatin, cisplatin, vincristine, methotrexate, paclitaxel, docetaxel, 5-fluorouracil, UFT, hydroxyurea, gemcitabine, vinorelbine, irinotecan, tirapazamine, or matrilysin*.

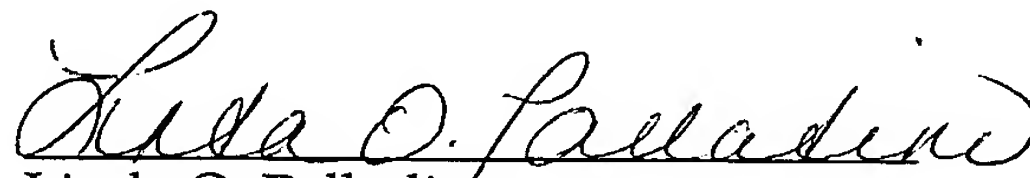
62. (New) A kit for causing tumor vascular endothelial cell death by targeting tumor vasculature in a mammal comprising a composition which comprises a molecule that detects ephrin-B2 coupled to an agent that causes vascular endothelial cell death, wherein the agent that causes vascular endothelial cell death is *gelonin, ricin A, ricin B, saporin, bryodin 1, bryodin 2, momordin, pokeweed antiviral protein from seeds (PAP-S), trichokirin, or abrin*.

There is absolutely no teaching or suggestion in Anderson et al for the emphasized claim limitations recited in new claims 43, 46 and 49 and kit claims 57, 58, 59, and 62. Thus, the third and final criterion for establishing a *prima facie* case of obviousness has not been met. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC §103(a).

**Fees**

A response to the Office Action that was mailed by the United States Patent and Trademark Office on April 21, 2003, is due on July 21, 2003, and as such this response is being timely filed. No fee is deemed necessary in connection with filing this paper. However, if any fee is necessary, please charge such fee to Deposit Account Number 18-0650.

Respectfully submitted



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